

REMARKS

The Applicants appreciate the Examiner's thorough examination of the subject application. Applicants request reconsideration of the subject application based on the following remarks.

Claims 1, 3-34 are currently pending in the application. Claims 1, 3-8, 10-25 have been amended and new claims 27-34 have been introduced. Claims 1, 3-8 and 10 have been amended to remove non-elected subject matter. Additionally, support for the amendment to variable Ar in claims 1, 3-7 is found throughout the specification. See, for example, page 8, lines 17-19 and the compounds listed from page 10, line 28 to page 14, line 3. Claims 27-34 are supported by the claims as originally filed. No new matter has been added by the amendments to the specification or the claims.

Claim 10 has been amended to correct a clerical error in naming compounds encompassed Group III. That is, the indication of "9-" has been replaced with "N-" at the beginning of certain compounds to indicate the correct point of attachment of the Ar-W- group to the diazepine ring. Support for the amendment may be found in claim 1 as originally filed.

The instant amendment incorporates the Abstract provided in copending international application PCT/US00/01968. Thus, the objection to the specification for the omission of an abstract should be withdrawn.

The specification was objected to because the Office Action alleges that the terms "alkyl," "alkenyl," and "alkynyl" cannot include cyclic groups. The objection shall be addressed in connection with alleged rejection of claims 1, 3-9, and 11-16 under §112, second paragraph.

The title of the invention has been amended as suggested by the Office Action. Thus, the objection to the title should be withdrawn.

Claims 10-26, as amended, and new claims 29-36 are in proper multiple dependent format. Thus, the objection under 37 C.F.R. 1.75(c) should be withdrawn.

Claims 1, 3-9, and 11-16 were rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject which applicant regards as the invention.

The language "optionally substituted" is not indefinite. One skilled in the art, will readily recognize that optionally substituted groups, such as optionally substituted alkyl groups, are intended to encompass those alkyl groups which, in certain embodiments, comprise one or more substituents on the alkyl chain. Moreover, Applicants clearly specify those groups from which additional substituents present as part of an optionally substituted group are selected. Page 8, line 20 to page 9, line 27 provides a list of groups from which such optionally present groups may be selected.

Claims 1 and 3-7 has been amended as suggested by paragraphs 11 and 12 of the Office Action.

The specification and claims were objected/rejected because the Office Action alleges that the terms "alkyl," "alkenyl," and "alkynyl" cannot include cyclic groups. The Office Action supports this position by citing a chemical dictionary published in 1977.

Applicants respectfully disagree.

Applicants note that the scope of the term "alkyl" is frequently used in such a manner to encompass cyclic groups in addition to linear and branched hydrocarbon residues. As is well known in the art, the terms alkyl is frequently used colloquially within the chemical arts to refer to either linear and branched aliphatic hydrocarbons or to linear, branched and cyclic aliphatic

hydrocarbons. The instant specification clearly specifies that the term "alkyl" is intended to refer to saturated linear, branched and cyclic hydrocarbon groups.

The use of the terms alkenyl by those trained in the chemical arts is also sufficiently flexible to allow for inclusion of cyclic groups as provided by the definition of "alkenyl" in the instant specification.

The definition of the term "alkynyl" provided by the specification, as amended, refers to non-cyclic groups, e.g., linear and branched alkynyl groups.

Thus, the definitions of the terms "alkyl," "alkenyl," and "alkynyl" are not repugnant to the usual meaning of these terms. Therefore, the objection to the specification should be withdrawn and claims 1, 3-9, and 11-16 are fully compliant with the requirements of 35 U.S.C. §112, including the requirements of §112, second paragraph.

Claim 5 was rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The assertion in the Office Action that nitrogen is only a trivalent atom is not correct. As is well known in the art, neutral nitrogen atoms comprise four sp^3 orbitals of which three orbitals are typically involved in bonding to other atoms and a fourth orbital is filled with a nitrogen lone pair. Thus, nitrogen is a tetravalent atom. More particularly, positively charged nitrogen atoms utilize all four sp^3 orbitals in bonding to other atoms. Thus, nitrogen atoms, which are present in an aromatic system, are capable of forming N-oxides or ammonium salts including N-protonated or N-alkylated azaheterocyclic groups (e.g., pyridinium or pteridinium salts) which comprise a cationic tetravalent nitrogen. Thus, the meaning of the language "optionally substituted nitrogen" would be clear and concise to one skilled in the art.

Claims 19-25 were rejected under 35 U.S.C. §112, second paragraph, as being allegedly incomplete for omitting essential steps.

Claims 19-25, as amended, provide for the step of administering to the patient an effective amount of a compound of the invention. Thus, claims 19-25 provide process step for the method of treatment of subjects or patients.

Claim 26 has been amended as suggested by paragraph 16 of the Office Action.

Claims 11-25 were rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not provide enablement for treating patients "susceptible to a" disease.

Applicants respectfully disagree. The specification provides that patients who are susceptible to disease include immunosuppressed patients. See, for example page 6, lines 16-25 and page 16, line 26 to page 17, line 4. The present invention further provides that immunosuppressed patients, such as AIDS patients (See, for example, (a) *J. Am. Med. Assoc.* **1988**, 259, 1185-1189; (b) *Ann. Intern. Med.* **1995**, 122, 755-761; (c) *J Infect.* 2001, 42, 8-15, copies of which are attached as part of an Information Disclosure Statement), and those undergoing immunosuppressive cancer treatment, which includes chemotherapy, radiation therapy, and the like, are particularly susceptible to parasitic infections.

Claim 17, as amended, provides methods of treating patients who have received or **are receiving** immunosuppressive cancer chemotherapy. Applicants believe that claim 17, as amended, obviates the rejection raised by paragraph 18 of the Office Action.

Thus, claims 11-25 are fully supported by the specification and comply with all of the requirements of 35 U.S.C. §112, including the requirements of §112, first paragraph.

Claims 1, 3, 5, and 8 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Mueslin (CH 372,675).

Claims 1, 9, and 26 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Marangos (European Journal of Pharmacology).

Claims 1, 3, 8, 9, and 26 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Kihara ('200).

Claims 1, 5, 8, and 26 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Andreani (European Journal of Medicinal Chemistry).

Claims 1, 3, 8, 9, and 26 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Ohshima (EP 549352 A2).

Claims 1, 3, 5, 8, 9, 11, 18, 19, and 26 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Garforth (Journal of Enzyme Inhibition).

Claims 1, 3, and 5 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Takami (JP 8-119920).

Claims 1, 3, and 5 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Beilstein (Ref AG).

Each of the rejections is traversed.

Claim 1, as amended, provides compounds in which Ar is a heteroaryl group having at least one amino group which may be optionally substituted with additional substituents.

None of the cited references teach or suggest compounds comprising a diazepine or dihydrodiazapine ring system coupled through a linker W to an optionally substituted heteroaryl group having at least one amino substituent.

Thus Claim 1 is patentable over the cited documents. Claims 3, 5, 8, 9, 11, 18, 19, and 26 depend from claim 1 and are therefore also patentable over each of the cited documents or any combination thereof.

Claims 19-24 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Wolff (Burger's Medicinal Chemistry).

Each of claims 19-24 provide methods of treatment which include the administration of a compound according to claim 1 or claim 10.

None of the compounds disclosed or suggested by Wolff satisfy structural requirements of Formula I in claim 1 nor are the Wolff compounds included among the compounds listed in claim 10. Thus, claims 19-24 are patentable over Wolff.

Claims 19, 20, 22, 23, and 25 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by RM Corwin (U. Missouri College of Veterinary Medicine).

The Office Action asserts that paragraph 19 teaches treatment of *T. gondii* infections in cats with pyrimethamine or clindamycin.


Regardless of whether the assertion made by the Office Action is true, neither pyrimethamine or clindamycin satisfy structural requirements of Formula I in claim 1 or are compounds listed in the Markush group of claim 10. Thus, claims 19, 20, 22, 23, and 25 are patentable over RM Corwin.

A. Rosowsky
U.S.S.N.: 09/890,112
Page 27

Early consideration and allowance of the application are earnestly solicited.

Respectfully submitted,

June 26, 2003



John B. Alexander, Ph.D. (Reg. No. 48,399)
Dike, Bronstein, Roberts & Cushman
Intellectual Property Practice
Edwards & Angell, LLP
P.O. Box 9169
Boston, MA 02209
Tel: 617-517-5557
Fax: 617-439-4170